REMARKS

Claims 1-7 and 12-24 are pending and under examination in this application. No amendments are made herein.

35 USC § 103

Claims 1-7 and 12-14 were rejected as allegedly being unpatentable over WO 00/38730 in view of Geiger et al., 2001, Cancer Res., 61:8513-19 ("Geiger"), Kaliński et al., 1998, J. Immunol., 161:2804-09 ("Kaliński"), and a material safety data sheet for NS-398. Applicants respectfully traverse the rejection for the reasons of record and for the following reasons.

WO 00/38730 discloses a method for treating or preventing a neoplastic disorder in a mammal by treating the mammal with a therapeutically effective amount of a combination of two or more components, wherein the first component is a COX-2 inhibitor and the additional component can include, among other things, a vaccine (see abstract and page 9). However, the term "vaccine" appears only three times in the entire document, and no evidence or rationale is provided as to why inhibition of COX-2 would be specifically useful in combination with a vaccine. WO 00/38730 does not disclose or make obvious the use of dendritic cells in a method for treating cancer, or the use of dendritic cells in combination with a COX-2 inhibitor.

Geiger discloses the use of immature dendritic cells that have been pulsed with tumor lysate in vitro (Office action, page 3). Geiger does not disclose the use of COX-2 inhibitors in combination with dendritic cells for treatment of cancers. Additionally, applicants respectfully disagree with the Office's interpretation of "unprimed" dendritic cells to encompass "those that have not been actively matured by in vivo culture (i.e. 'made ready' for activating T cells" (Office action, page 3). During examination, claims should be given their broadest reasonable construction in light of the specification as it would be interpreted by one of ordinary skill in the art. See *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316, 75 USPQ2d 1321, 1329 (Fed. Cir. 2005) and MPEP § 2111. Further, the broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. *In re Cortright*, 165

F.3d 1353, 1359, 49 USPQ2d 1464, 1468 (Fed. Cir. 1999). See also MPEP § 2111. Although the specification does not provide explicit definitions of the terms "primed" and "unprimed", applicants submit that the specification makes clear to one of skill in the art that primed dendritic cells are those that have been exposed to antigens and that have, e.g., acquired, processed, and/or been loaded with the antigens, whereas unprimed dendritic cells are those that have not acquired, processed, and/or been loaded with antigens. See, e.g., paragraphs [0044] and [0045] of the specification. As all of the dendritic cells used in Geiger had been pulsed with tumor cell lysates, Geiger does not teach or suggest the administration of unprimed dendritic cells.

Kaliński does not remedy the deficiencies of WO 00/38730 and Geiger. Kaliński is directed to investigating mechanisms of endogenous dendritic cell maturation in vivo. Kaliński provides no teaching or suggestion of the effect of PGE_2 or COX-2 inhibitors on exogenously administered dendritic cells (e.g., primed or unprimed dendritic cells). Based on the limited disclosures of WO 00/38730, Geiger, and Kaliński with regard to the claimed subject matter, applicants submit that the claims would not have been obvious in view of WO 00/38730, Geiger, and Kaliński. Accordingly, applicants request reconsideration and withdrawal of the rejection of claims 1-7 and 12-14 for alleged obviousness.

Claims 1, 3-7, 12, 14-15, 17-22, and 24 were rejected as allegedly being unpatentable over WO 00/38730 in view of US 7,240,982, Zeidler et al., 2000, FASEB J., 14:661 668 ("Zeidler"), and a material safety data sheet for NS-398. Applicants respectfully traverse the rejection.

As noted above, WO 00/38730 discloses a method for treating or preventing a neoplasia disorder in a mammal by treating the mammal with a therapeutically effective amount of a combination of two or more components, wherein the first component is a COX-2 inhibitor and the additional component can include, among other things, a vaccine (page 9). However, the term "vaccine" appears only three times in the entire document, and no evidence or rationale is provided as to why inhibition of COX-2 would be specifically useful in combination with a vaccine. WO 00/38730 does not disclose or make obvious the use of mature dendritic cells in a

method for treating cancer, or the use of mature dendritic cells in combination with a COX-2 inhibitor.

US 7,240,982 discloses a method for inhibiting proliferation of cancer cells that includes contacting the cancer cell with a vaccine (e.g., a dendritic cell vaccine) that includes a GDOX peptide (see abstract, col. 21-22). US 7,240,982 does not disclose or make obvious the use of dendritic cells (e.g., mature dendritic cells) in combination with a COX-2 inhibitor.

Regarding Zeidler, the Office action states (at page 6):

> Zeidler et al. teach that PGE2 production by tumor cells can contribute to immune evasion by downregulating MHC expression in the tumor cells and by inhibiting the function of tumor infiltrating T cells (see page 666, in particular).

Applicants respectfully disagree. Zeidler discloses experiments demonstrating that PGE_2 causes down-regulation of CCR5 and Mac-1 on monocytes, leading to reduced endothelial cell adherence and migration in response to chemoattractants (see abstract, page 666, left col.). Zeidler does disclose that tumor cells down-regulated MHC molecules (see page 666, left col.), but this effect is not attributed to PGE_2. In fact, Zeidler states that MHC class I expression levels were not affected in its experiments (page 666, right col.). Additionally, applicants find no disclosure in Zeidler that PGE_2 inhibits the function of tumor infiltrating T cells. Rather, Zeidler speculates that the effect of PGE_2 on monocyte adherence and migration is responsible for a decrease in the number of tumor infiltrating leukocytes (see page 666, right col.).

However, the Office's alleged case of obviousness relies, at least in part, on this assertion. Thus, the Office is mistaken in its conclusion that "Zeidler et al. teach that tumor derived PGE-2 decreases tumor MHC expression and inhibits T cell function" (Office action, page 6). As this is not the case, applicants submit that a *prima facie* case of obviousness has not been made. For a prima facie case of obviousness, the content of the cited art must be correctly determined, which is not the case here. See MPEP 2141.01. Accordingly, applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 3-7, 12, 14-15, 17-22, and 24 for alleged obviousness.

Claims 2, 13, 16, and 23 were rejected as allegedly being unpatentable over WO 00/38730, US 7,240,982, Zeidler, and a material safety data sheet for NS-398, as described above, and further in view of US 6,300,090 and Kikuchi et al., 2001, Cancer Immunol. Immumother., 50:337-344 ("Kikuchi").

The disclosures of WO 00/38730, US 7,240,982, and Zeidler are discussed above. Neither US 6,300,090 nor Kikuchi, alone or in combination, remedies the deficiencies of WO 00/38730, US 7,240,982, and Zeidler. Therefore, applicants respectfully request reconsideration and withdrawal of the rejection of claims 2, 13, 16, and 23 for alleged obviousness.

35 USC § 112, first paragraph

Claim 16 was rejected as allegedly not in compliance with the enablement requirement. The Office action (at page 8) alleges that claim 16 "is drawn to a method for treating cancer comprising administering a mature 'unprimed' dendritic cell." However, claim 16 contains no recitation of an unprimed dendritic cell. Applicants request clarification and withdrawal of the rejection of claim 16.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is hereby respectfully requested.

Applicants do not concede any positions of the Office that are not expressly addressed above, nor do applicants concede that there are not other good reasons for patentability of the presented claims or other claims. Specifically, applicants do not concede that the cited references disclose the limitations of the dependent claims.

This response is being submitted with a Petition for Extension of Time and the required fee. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 22862-0003US1.

Respectfully submitted,

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